



A Case of Suspected COVID-19 Identified with AIDS, PCP and Tuberculosis

AIDS, PCP ve Tüberküloz Tanıları Alan COVID-19 Şüpheli bir Olgu

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Abstract

HIV (Human Immunodeficiency Virus) is the virus that causes AIDS (Acquired Immune Deficiency Syndrome), while PCP (Pneumocystis jiroveci pneumonia), tuberculosis, CMV (Cytomegalovirus) and candidiasis are the OIs (opportunistic infections) occurring due to immune deficiency. OIs, and bacterial pneumonias in particular, are the most common causes of mortality, which makes the screening and prophylactic therapy for OIs necessary. The synergy between tuberculosis and HIV has long been known, and worsens the prognosis. PCP is an OI that is caused by a fungus named *P. jiroveci*. COVID-19 has emerged as a new cause of death among AIDS patients. Screening and prophylactic therapy for OIs is vital for patients with AIDS, however, mortality may be high due to delays in screening and prophylaxis in those whose HIV positivity is detected coincidentally. We report here on a patient who applied to our hospital with suspected COVID-19 pneumonia who was found during follow-up to be HIV positive with PCP and pulmonary tuberculosis.

Key words: HIV, PCP, Tuberculosis, Covid-19.

Öz

HIV (İnsan İmmün Yetmezlik Virüsü) immün sistemi zayıflatan, AIDS (Kazanılmış Bağışıklık Yetersizliği Sendromu) hastalığına yol açan viral bir enfeksiyondür. İmmün sistemin zayıflaması ile birlikte, tüberküloz, PCP (Pneumocystis jiroveci pnömonisi), CMV (sitomegalovirüs), kandida gibi fırsatçı enfeksiyonlara olanak sağlamaktadır. En yüksek mortaliteyi oluşturan durumlar fırsatçı enfeksiyonlardır. Bu durum AIDS hastalarında fırsatçı enfeksiyonlara yönelik tarama ve profilaksi uygulanmasını gerekli kılmıştır. Tüberküloz ile HIV birlikteliği uzun zamandır bilinmekte ve prognozu kötüleştirmektedirler. PCP ise günümüzde mantar olarak kabul edilen *P. jirovecii* etkenli fırsatçı bir pnömonidir. Covid -19 pandemisi ile birlikte de AIDS hastalarında yeni bir mortalite sebebi ortaya çıkmıştır. AIDS hastalarının bu fırsatçı enfeksiyonlara karşı taranması, profilaktik tedavi alması ve erkenden tedavi almaları hayati önem taşımaktadır. Ancak HIV pozitifliği rastlantısal olarak saptanan kişilerde tarama ve profilaksi gecikmesinden ötürü mortalite yüksek seyredebilmektedir. Bu yazıda Covid-19 pnömonisi şüphesi ile hastanemize başvuran bir hastanın HIV pozitif tespit edilip PCP ve takibinde akciğer tüberkülozu saptanması anlatılmaktadır.

Anahtar Sözcükler: HIV, PCP, Tüberküloz, Covid-19.

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Human immunodeficiency virus (HIV) is a viral infectious disease that weakens the immune system and affects blood cells, especially CD4-T lymphocytes (1). HIV remains as a growing health problem worldwide. According to the World Health Organization (WHO), 38 million people worldwide were infected with HIV in 2019, while a total of 75 million people have died of acquired immune deficiency syndrome (AIDS) since the epidemic began (1). Due to the immunodeficiency associated with AIDS, opportunistic infections and some cancers are common, including tuberculosis (TB) and *Pneumocystis jirovecii* pneumonia (PCP). Accordingly, WHO suggests screening for TB and other opportunistic infections in patients with HIV (1,2). There is a synergistic relationship between TB and HIV positivity (3,4).

PCP is the most common infectious disease in AIDS. *Pneumocystis jirovecii* is the microbiological fungal pathogen that causes PCP (5).

Mortality in AIDS has decreased as a result of screening tests for infections and antiretroviral treatments (ART) (5,6). Today, only those who are unaware of their HIV positivity can contract such opportunistic infections (6).

In December 2019, a SARS Cov-2 virus outbreak in Wuhan, China led to a pandemic that came to affect the world, and the resulting COVID-19 disease has become the highest cause of mortality in AIDS patients. The clinical findings and radiological images of COVID-19 can be mistaken for opportunistic infections in HIV-positive patients, leading to a new problem in the form of treatment delays (7).

Our case presented with the clinical and radiological suspicion of COVID-19 pneumonia, but was subsequently diagnosed with AIDS and PCP. During treatment for ART and PCP, the patient was also found to have TB.

CASE

Our 63-year-old male patient was born in Bartın, Turkey, and was employed as a construction worker. He had no chronic disease and did not use drugs, but had a 40-pack years smoking history.

He presented at Ankara City Hospital with complaints of shortness of breath, cough, sputum for 2 months and diarrhea for 2 weeks. And weight loss of 5 kg in 2 months. A radiograph of the posterior-anterior chest revealed infiltration extending from the vertebrae to the periphery under the right hilar region (Figure 1). Thoracic computed tomography (CT) revealed a millimetric nodule in the

middle lobe of the right lung with a diffusely ground-glassed bilateral appearance (Figure 2 and 3). Interstitial lung disease and COVID-19 pneumonia could not be differentiated in the city hospital, and so the patient was referred to us.

Upon physical examination, the patient's general condition was good, blood pressure was 110/70 mmHg, heart rate was 108 beats/min, respiratory rate was 20, fever was 38.3°C, oxygen saturation in room air was 97% and respiratory sounds were decreased bilaterally.

Laboratory tests revealed hemoglobin 13.8 g/dl, creatinine 1.29 mg/dl, GFR 60.3%, serum lactate dehydrogenase (LDH) 453 IU/L, C-reactive protein 74 mg/L, ferritin 1612 ng/ml and d-dimer 0.88 mg/L.

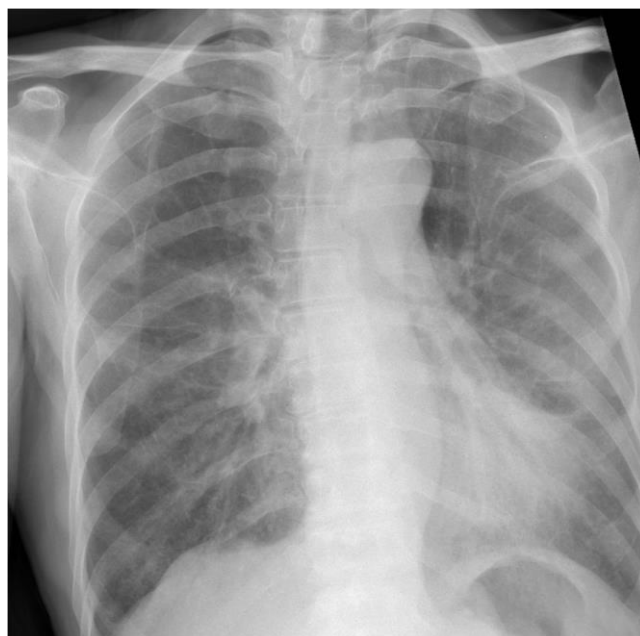


Figure 1: Chest X-ray of the patient at the time of admission

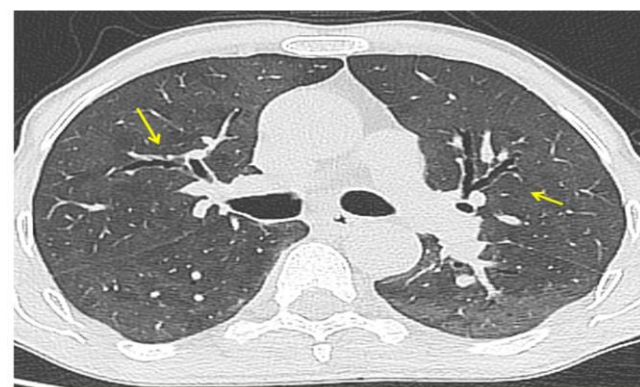


Figure 2: A patient thorax tomography revealing the dark bronchus sign image that is characteristic of PCP

The patient was admitted to the hospital with suspected COVID-19 disease, however two COVID-19 polymerase chain reaction (PCR) tests were both negative. The patient was treated with favipiravir, enoxaparin sodium, ipratropium bromide, salbutamol and ceftriaxone. After an anti-HIV test result came back positive, the patient was consulted with the infectious diseases doctor. The patient was considered to have PCP, and ceftriaxone was switched to trimethoprim-sulfamethoxazole (TMP-SMX) treatment. After the PCP PCR test was positive, the patient was referred to the infectious disease service.

Upon follow-up, the patient's CD4 count was 135/mm³ and PCP direct fluorescent antibody was positive, and treatment was started with emtricitabine, tenofovir alafenamide and bictegravir, in addition to treatment with TMP-SMX. During follow-up, the patient's oxygen saturation at room air declined to 66%, fever was 38.5°C, and blood cultures were all negative. The patient, who was unable to provide a sputum sample, was referred to us again for fiberoptic bronchoscopy (FOB), bronchial lavage acid-fast staining (AFS) and bronchial lavage Xpert MTB/RIF (rapid PCR test). The patient's bronchial lavage AFS smear was negative, while the Xpert MTB/RIF test detected *Mycobacterium tuberculosis* (MTB) and rifampicin was susceptible. Fifteen colonies were grown in the culture, and MTB were detected that were sensitive to Isoniazid (H), Rifampicin (R), Streptomycin (S), Pyrazinamide (Z) and Ethambutol (E) on the antibiogram. The patient was diagnosed with HIV+, Xpert MTB/RIF positive new case of pulmonary tuberculosis and treated with H, R, E and Z. The patient's fever did not return after TB treatment. Nausea and vomiting were found in relation to the isoniazid intake, and gastrointestinal intolerance of the drug was diagnosed, and so treatment with R, E, Z, and moxifloxacin was started.

A post-TB diagnosis CT showed bilateral diffuse micrographs that had increased significantly when compared to the previous CT, indicating PCP (Figure 4).



Figure 3: Dark bronchus sign and bilateral diffuse ground-glass densities in the patient thorax tomography

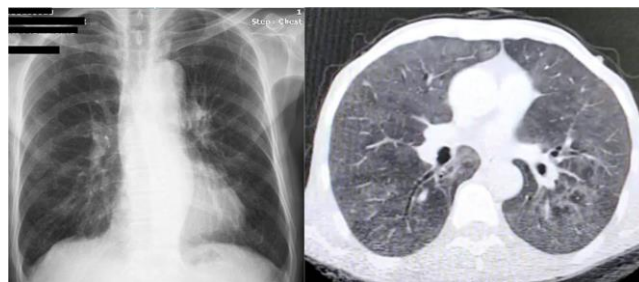


Figure 4: Imaging of the patient after diagnosis with tuberculosis

DISCUSSION

Since the sensitivity of COVID-19 PCR tests in the early phase of the disease is 71%, patient was started on favipiravir treatment for COVID-19 pneumonia based on their complaints on admission and the ground-glass images on CT, even though the COVID-19 PCR test was negative (8). The ground-glass images on the patient's CT, however, were not typical of COVID-19 pneumonia, and the patient's symptoms and radiological imaging were actually attributable to the patient's diagnosis of HIV and PCP during hospitalization. It was assumed that the patient did not have COVID-19 pneumonia.

With the advances in HIV treatment, mortality from the disease has declined, although as opportunistic infections occurring alongside HIV infection can lead to death, screening, prophylaxis, early diagnosis and treatment must be carried out thoroughly in HIV patients (1).

It is well known that those with HIV-infections are at high risk of developing TB, and that a synergistic relationship exists between the two (3,9). DeRiemer et al. (10) reported that the probability of developing pulmonary TB in HIV-positive individuals is 8 times higher than in non-HIV-positive individuals. To date, more than 40 million people have lost their lives due to the comorbidity of HIV and TB, which necessitates screening and prophylaxis for TB in those who are HIV positive. The tuberculin skin test (TST) and interferon-gamma release assays are used for the screening of tuberculosis in HIV-positive patients. It is important to remember that HIV-infected patients must be considered immunosuppressed when interpreting TST results, and so results of 5 mm and above should be considered positive. In Turkey isoniazid is given for 9 months as TB prophylaxis as the first choice. Imaging of the lungs in immunocompromised patients, such as those who are HIV-positive, may be normal, or there may be such atypical findings as pleural fluid, pneumothorax, mass lesions and miliary shadows. Our patient did not have typical imaging for TB. AFS, Xpert MTB/RIF or the TB culture of specimens can be used for diagnosis. The bacteriological positivity rate is lower in HIV positive TB

patients than in immune competent TB cases. In recent years, a serological urine test has been developed for lipoarabinomannan for TB diagnosis in HIV-positive patients. The duration of TB treatment in HIV-positive patients is 6 months (9). Mortality in multidrug-resistant TB patients is increased in HIV patients (3). Drug susceptibility testing should be performed as soon as possible and appropriate treatment should be started early. Non-tuberculous Mycobacteria (NTM) infection is also more common in HIV-infected patients than in non-HIV patients, although MTB is more common than NTM in HIV patients. Some HIV-TB patients who take their medications regularly and respond well to treatment may experience radiographic and clinical deterioration, which is a condition referred to as immune reconstitution inflammatory syndrome (IRIS) that is associated with the recovery of immunity. Our patient did not develop IRIS. Antiretroviral treatment and tuberculosis treatment should be continued together without interruption (9). Studies have shown mortality to be lower in patients treated with ART in the early period after starting anti TB treatment (9,11), although ART may interact with anti-TB drugs, especially rifampicin, which may be replaced with rifabutin.

PCP is an opportunistic infectious disease that occurs in immunosuppressed patients, and can be mortal in HIV positive patients in whom it develops when the CD4 T lymphocyte count falls below 200/mm³. In our case, the CD4 count was 135/mm³. Patients may develop non-specific symptoms such as fever, cough, sputum and shortness of breath (5,6), while our patient had shortness of breath, cough, fever, and diarrhea. As the patient was examined during the COVID-19 pandemic, COVID-19 pneumonia was initially thought to be present. Imaging of the patient's lungs may be normal, although pneumothorax, especially in HIV-positive individuals, should be suggestive of PCP (6). *P. jirovecii* does not grow in cultures. A definitive diagnosis can be confirmed based on morphological evidence of the microorganism in bronchoalveolar lavage (BAL), with sputum collected by FOB. Immunofluorescence staining with fluorescently labeled monoclonal antibodies is considered the optimum means of diagnosis. In some studies, an LDH level of >500 IU/L has been shown to have a poor prognosis in PCP (6). Our patient's LDH level was 453 IU/L. TMP-SMX is recommended as a prophylaxis and for treatment of pneumonia in HIV-positive patients with PCP. Dose adjustment is important in treatment, with TMP 15-20 mg-SMX 75-100 mg/kg/day IV being given in 3-4 doses. It has been reported that treatment with corticosteroids in patients with

hypoxia has a positive effect on prognosis (6). While receiving TMP-SMX treatment for PCP, outpatient also received corticosteroid treatment due to hypoxia, and emtricitabine, tenofovir, alafenamide and bictegravir as antiretroviral treatments.

In a study by Castro et al. (12), the coexistence of PCP and TB was observed in 5.8% of a total of 2,651 HIV positive patients, while a study by Tchatchouang et al. (13) revealed the coexistence of PCP and TB in 10% of a total of 211 HIV positive patients. TB shouldn't be forgotten, as radiology may not be typical or may even be normal in HIV positive patients. Although radiology is typical for PCP, as in our patient, TB treatment was initiated as a result of the patient's positive TB PCR and positive culture. In summary, a patient who was thought to have COVID-19 pneumonia was diagnosed with HIV positivity, PCP and TB, and was treated successfully.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - Z.T.S., Ş.Ö.; Planning and Design - Z.T.S., Ş.Ö.; Supervision - Z.T.S., Ş.Ö.; Funding - Z.T.S.; Materials - Z.T.S.; Data Collection and/or Processing - Z.T.S.; Analysis and/or Interpretation - Z.T.S.; Literature Review - Z.T.S.; Writing - Z.T.S.; Critical Review - Z.T.S.

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